

## BILATERAL POLYCYSTIC DEGENERATION OF THE KIDNEYS\*

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The title of this paper should indicate a degeneration of the kidneys that is quite rare and equally fatal. The first case I find recorded in the library of the Surgeon-General's office, according to the index catalogue thereof, was reported in London in 1827, by Jeffreys.

*Synonyms.*—Various names have been applied to this condition, Rayer gave it the name of "cystic degeneration of the kidneys;" Cruvelhier, "cystic metamorphosis, or transformation of the kidneys," while others have given it the titles, "cystic disease," "congeries of renal cysts," "conglomerate cysts," and "large polycystic kidney."

*Definition.*—The condition under consideration is not to be confounded with the cystic condition often seen in chronic interstitial nephritis and is also to be distinguished from other cyst formations of this organ often occurring singly or in a small number, having perhaps prodigious proportions and usually arising from obstruction of a ureter or kidney calices and which are not commonly bilateral. This form of disease, *per contra*, is usually bilateral though often developed unevenly in the two kidneys. Usually one kidney shows marked enlargement while palpation and even inspection, as well as analysis of separated urines may lead to the opinion that little or no involvement of the fellow kidney exists. Many times has a large polycystic kidney been extirpated under the misapprehension that the fellow was healthy and competent and a fatal result from uremia followed in a few days or weeks. Nor is the kidney on one or both sides always materially enlarged, though no-

table enlargement is usual. Dickinson studied 26 cases finding but one kidney free of it. Lejars failed to find a normal kidney in 62 cases and Ritchie found that in 82 cases he had studied post mortem, the condition was unilateral in but two. Henry Morris operated on 7 cases in 4 of which a normal kidney was found on the opposite side. The characteristics of the bilateral polycystic kidney, then, are an organ practically retaining its shape, but being changed in size to any dimensions up to ten or twelve times the normal ones, degenerated into a mass composed of cysts numbering hundreds or thousands, that vary in size from microscopic measurements to those having capacity for several quarts of fluid, and with contents quite characteristic, as will be mentioned in considering the pathology of the condition.

The history of bilateral polycystic degeneration of the kidneys extends to the case reported by Jeffreys in 1827 and the comparatively small amount of literature on the subject is quite disappointing. Lejars collected 68 cases and several have since been reported. Bunting, in 1900, collected 200 cases. I believe a conservative estimate of the number of reported cases would be less than 300. A question that has not been settled by clinicians and pathologists is whether the large polycystic kidney weighing one to sixteen pounds (Hare's case) is the same as the congenital polycystic kidney found before and a short time after birth.

I have observed the following case: Mrs. H. B——, age 29 years, was admitted to my service in Columbia Hospital, July 17th, 1908,

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on account of a general anemic condition accompanied by a cough and agalactia. During the three days residence in the hospital not more than four ounces of urine containing pus was obtained by catheterization. She exhibited twitching of the extremities, which rapidly developed into marked tremor, sank into uremic coma and died on the 20th inst. Sixteen days previously she had given birth to a child and the labor was reported normal.

Dr. John S. Neate, assistant pathologist of the hospital and anatomist to the Army Medical Museum, has carefully studied the specimens from 10 cases, including my own, his report on the autopsy in my case is as follows: The body showed only a moderate degree of emaciation, the skin somewhat jaundiced and rigor mortis present. On opening the abdomen the peritoneum and intestines were found to be normal, but occupying each outer third of the cavity from the under surfaces of the liver and spleen superiorly down to or below the crests of the ilia were found enlarged cystic kidneys. The weight of the kidneys taken together was 80 ounces, length,  $8\frac{1}{4}$ -in.; width,  $4\frac{1}{4}$ -in.; thickness, about 4-in., both being symmetrically enlarged and about equal in size. The cysts varying in size from that of a pea to that of a walnut, were seen through the peritoneal covering filled in most cases with a straw-colored fluid and in others with dark brown or reddish coagula. The ureters were traced from the bladder to the pelvis and were normal in size. On section the left ureter oozed a few drops of pus. The bladder contained a few ounces of pale fluid containing pus threads, but there was no inflammation of the bladder wall and the ureteral orifices were normal. The kidneys exhibited no adhesions to the neighboring intestines and the blood vessels appeared to be in their normal relations, but larger than usual. On section several ounces of fluid escaped and the kidney was found to be a mass of closely packed cysts with thin fibrous septa and little or no normal kidney tissue visible. Some few of

the cysts contained thick pus. The liver was pale, mottled with yellowish areas and rather bloodless (as, indeed, were all the organs) but contained no cysts. The spleen was slightly enlarged and firm. The contents of the thorax was normal, except the heart, which was slightly enlarged. The uterus and appendages were in good condition. Cultures made from the pus in the kidney gave capsulated diplococci and common pyogenic organisms.

Anatomical diagnosis: Bilateral congenital cystic disease of the kidneys with secondary infection. On removal to the laboratory the organs were submitted to closer examination and it was found that a large sized probe could be passed with ease through the ureters into the pelvis. The plainly visible cysts were counted as they appeared on the convex surfaces of each half of the kidneys and were found to average 250, while the cut surfaces gave 20 to 30 less in number. The infundibula were explored and several cysts were found, probably of recent origin, which opened therein, and distributed around these sinuses were the small irregular triangular areas not apparently occupied by cysts and containing the remnants of the kidney tissue proper. A liberal estimate of the solid tissue containing glomeruli and convoluted tubules in anything like normal arrangement taken altogether in one of these kidneys would not exceed one cubic inch of normal kidney cortex. While the larger cysts are about one inch in diameter and range downwards from marble to pinhead and finally microscopic size, there is a certain uniformity in size and distribution which is suggestive. The smaller cysts occupy the triangular areas where the septa join, and between these again microscopic cysts were subsequently found. This economy in distribution, taken together with the fact that the sound tissue is in immediate relation with the pelvis and that all semblance of pyramids is obliterated, leads one to the conclusion that the process of cyst formation is gradual, continuous, and proceeds from the cortex inwards,

the area around the infundibula being the last to succumb. From the extreme thinness of the walls of the larger cysts one wonders that they have not coalesced to form a few large ones, and the inference is inevitable that the internal pressure must have been low or very equally counterbalanced by external pressure.

Dr. W. M. Gray, microscopist of the Army Medical Museum made the microscopical sections and the photographs, as well as the photomicrographs accompanying this report, which latter is as follows: The organs are made up of a soft spongy mass consisting of innumerable cysts varying in size from those of microscopic dimensions to those of the size of an English walnut. These cysts are filled with a semi-jelly-like albuminous fluid and urine; the walls of the cysts have a framework of rather dense fibrous connective tissue. The septa dividing the cysts one from another is composed of this dense fibrous tissue, with an occasional aggregation of small round cells. Running through the septa are numerous tubules and glomeruli; the majority of which are enormously dilated and there is every indication that the cysts have developed both from the tubules and the glomeruli. Many of the tubules and also the smaller cysts are lined by a very pronounced columnar epithelium, which is quite distinct from the epithelium found in normal kidney tubules. The photomicrograph shows one of the dilated glomeruli and a small cyst, the latter partly filled by the jelly-like albuminous material. This cyst probably originated from a tubule. The photomicrograph also shows other smaller dilated tubules surrounded by dense connective tissue.

Microscopical examination of these cysts and the intercystic tissue disposes one to classify them as primary and secondary; those which obviously have existed for some time and those of recent development. There is no sharp line of transition from one type to the other, but in view of the probable origin

and effect of these cysts, it is helpful to an appreciation of the pathology and etiology of a condition all too obscure at the best. The oldest cysts have quite dense fibrous walls staining deeply with eosin, sometimes devoid of, or showing only vestiges of altered epithelial lining, and the adjacent tissue is rich in connective tissue, permeated by few tubules and these atrophied. The cysts of more recent formation contain cell detritus and fragmented nuclei and their walls contain little or no fibrous tissue. The neighboring tubules, chiefly of the collecting type, are flattened or pushed to one side in the process of their development, and the epithelium lining both cysts and tubules is of the low cubical order, practically identical in each of them. The inter-cystic tissue is relatively rich in tubules and contains but little connective tissue. The oldest cysts having dense fibrous walls are by no means the largest. In this kidney one is impressed by the persistence of straight tubules in the septa and the epithelium of the low cubical type, very regularly arranged with large nuclei staining intensely with hematoxylin. This type of epithelium is found replacing that of the convoluted tubules and in Bowman's capsules. In the few convoluted tubules and tufts which have escaped obliteration the transition is beautifully shown. In some areas the characteristic epithelium of the convoluted tubules has been shed in masses into the lumina and beneath it a new layer of the cubical type has formed. This type of cell, while it resembles somewhat those lining the ascending portion of the loops of Henle, is probably a reversion to the embryonic type. The few small islands of cyst-free tissue in the neighborhood of the calyces is rich in connective tissue and resembles the condition of chronic interstitial nephritis, except that there is a healthier appearance to the epithelium and an absence of change in the walls of the blood vessels. The intercystic tissue is everywhere surprisingly vascular. Distended capillaries or sinuses exceeding six or seven times the

normal size are found in close relation with tubules or penetrating islands of fibrous tissue; their walls consisting of a layer of flattened endothelial cells only and sometimes seven or eight of them aggregated so closely that their walls are in contact. Similar dilated spaces lined with endothelium, but containing no blood cells, were observed and in-

eration by the ever encroaching fibrous tissue may, in part, explain the cardiac hypertrophy which accompanies this condition. A few small interstitial hemorrhages readily account for the color in the coagula found in some of the cysts and from these in a similar case Sollman, by chemical analysis obtained the derivatives of hemoglobin, but no urea. The



Photograph of Bilateral Polycystic Kidneys.

terpreted as dilated lymph channels. The reason for an increased blood supply to such a mere shell of an organ, which consisted so largely of fibrous tissue, is hard to explain. The increase of connective tissue may account for the dilatation and contortion of the capillaries and lymph spaces described above and the increased blood pressure necessary to fill these sinuses and to preserve them from oblit-

liver exhibited a moderate amount of fatty change, chiefly located in the peripheries of the lobules. The bile ducts appeared to be reduplicated and some of them were distended and, in general, were surrounded by more than the usual amount of connective tissue, but no cysts were found. Adding to the complexity of the histological picture are the evidences of the very recent bacterial infection

which contributed to the fatal termination and are so well known as to require no description here.

*Pathological Anatomy.*—In the polycystic kidney the whole structure of the organ seems to be affected and the glomeruli are oft-times found to be practically all destroyed. In my case, studied by Neate, an estimate of the functioning kidney tissue was made and was thought to be not in excess of one cubic inch in each kidney. It is undoubtedly the uniformity of the process throughout the kidney that preserves the shape of the organ. Beck counted more than 100 cysts, on the surface of a kidney. On the surface of one of the kidneys in my case 250 cysts were counted and on the cut surface still many more were found. Sometimes the size of the organ is increased remarkably. In my case the kidneys weighed 80 ounces and each measured  $8\frac{1}{4}$  by  $4\frac{1}{4}$  by 4 inches. Danforth found the kidneys in his case weighed respectively  $5\frac{1}{2}$  and 6 pounds. In Hare's specimens the left kidney weighed 16 pounds and was  $15\frac{1}{4}$  inches in length, the right being double its normal size. The cysts occupying both the medullary and cortical substance alike project to the surfaces and push out the capsule as nodules. The cysts may be enormous and contain half a pint of fluid, which may vary from a very thin watery fluid to a thick and grumous one or even nearly pure blood. As will be noted the structure of the kidney is almost entirely transformed, there being left in my case an estimated cubic inch of renal functioning tissue in each one of the kidneys and it was in immediate relation to the pelvis. The kidney seems to be a mass of cysts separated by connective tissue. The oldest cysts have quite dense fibrous walls and show absence or only vestiges of a changed epithelial lining and the adjacent frame work is largely connective tissue containing a few atrophied tubules. The newer cysts contain debris recognizable as broken down cells, fragmented nuclei and walls containing but little

or no fibrous tissue. The neighboring tubules, chiefly of the collecting type, are flattened or pushed to one side in the process of their development and the epithelium lining both the cysts and the adjacent tubules is of the low cubical order and practically identical. The intercystic tissue is relatively rich in tubules and contains but little connective tissue. The largest of the old cysts do not invariably have the thickest walls. The normal epithelium of the convoluted tubules and in Bowman's capsules is seen to be replaced by the low cuboidal epithelium mentioned. The few small islands of cyst-free tissue adjacent to the calyces are rich in connective tissue resembling chronic interstitial nephritis, except the epithelium has an appearance nearer normal and absence of degenerative change in the blood vessel walls. Marked vascularity of the kidney frame work is everywhere apparent and hypertrophy of the left heart is quite commonly observed as a complication. The distended capillaries or sinuses everywhere observable have a layer of flattened endothelial cells only and sometimes seven or eight of these vessels are found in contact. Large spaces lined with endothelium, but containing no blood cells, are here noted and are probably lymph spaces. Numerous cases of this condition associated with cysts of the liver have been reported. Lejars found this complication was present in 17 of the 62 cases he tabulated. Ritchie found that in 82 cases the liver was cystic in 21, in one of which the thyroid, one the uterus, and one the ovary, was also cystic. Still's statistics would indicate that cystic degeneration of the liver rarely complicates congenital cystic kidney, for in 35 cases of cystic disease of the liver associated with cystic kidneys only 3 occurred in infancy. Cysts of the spleen have been observed as a complication. Henry Morris mentions the coexistence of talipes, cleft palate and imperforate anus as well as the absence of the anus, rectum, urethra and external genitals. He also notes the absence of the renal pelvis and the ureter. Newman found the

heart hypertrophied in 60 per cent. of the 105 cases he tabulated and the arteries atheromatous in one-fourth as many. He also observed malformations of the aortic valves and of the septum of the ventricle.

*Character of the Contents of the Cysts.*—The contents of the cysts vary greatly in different cases, and in different parts in the same case. The color is quite commonly straw, then serous or limpid. But it may be

rarely leucin. That the polycystic kidney is always a congenital condition, as believed by Henry Morris, I cannot accept, though believing it to be so with certain exceptions. One cannot ignore, or consider entirely disproven, the various theories that have been offered as to the origin of this condition. Of these there are four principal ones, viz.:

1. Persistent germinal rudiments—that is, foetal inclusions.
2. The obstruction theory



Photomicrograph of a section of Bilateral Polycystic Kidney x 150.

yellowish, purplish or, if hemorrhage has occurred, dark red. It may also be thick, viscid, turbid or colloid. The contents of some have been found to resemble pea soup, to be caseous and practically solid in other instances. Pus has been detected as a constituent of the contents. Usually the reaction is alkaline, but it may be acid or neutral. A large proportion of albumen is usually present with a small amount of urea, triple phosphates, cholesterin, uric acid, epithelium, fat, blood corpuscles and

which insists the development of the cysts is a sequel to a renal sclerosis that constricts the tubules or obliterates the papillae. 3. That there is a colloid or fatty change and that the cysts are centers of the change. 4. The neoplastic theory. Were the first theory sufficient to cover all cases the congenital influence would be at once unqualifiedly recognized, but with the proof of cirrhosis as a cause great difficulty at once arises in accepting the inflammatory process as being always

antenatal. In my judgment a very large proportion of the cases are due to the first named theory. That the Wolffian body forms the ureter and calyces and the metanephric blastema the urine-forming part of the kidney is amply demonstrated by Kolliker and other embryologists. That a failure of fusion of these two structures occurs is readily acceptable in the light of developmental anomalies so frequently observed in other parts of the human body. Moreover, such anomalies are frequently coexisting with the bilateral polycystic kidney. One can also understand how the anomaly may rarely exist on one side only. I have already stated how rarely this occurs. These facts are well known, viz.: That it frequently is found at child birth, and as a cause of dystocia, as reported by Morse and others, and frequently in the same family, a matter of common observation. It has very frequently been noticed that several children in a family will be victims of this disease. Beck found it in two sisters, Lund, in a man whose mother was a victim of it. Virchow reported cases in which 4 out of 6 children in the family were affected. Sanger also reports having observed families in which the first, fourth, seventh, tenth and thirteenth children had bilateral congenital cystic disease of the kidney, the other children being normal. Osler has written on this subject as have numerous others, but to me it appears that usually the disease arises from an inherited tendency toward faulty development, which frequently is not limited to the kidney. That this defective development appears in other parts of the urinary system we have only to mention exstrophy of the bladder with its frequent accompaniment of epispadias, etc. Nevertheless, one has to admit that antenatal cirrhosis being extremely rare and the presence of it, perhaps in a modified form, in the adult cases the conclusion is inevitable that the cirrhosis is the cause of the illness. Again knowing the proneness of the kidney to contain adrenal "rests" and hypernephroma develop in con-

sequence, to me it seems highly probable that this form of tumor, while not easily diagnosed, can form in the kidney from degeneration of such rests. The obstruction theory is plausible, but not always attractive. Some cases clearly develop in adult life from obstruction of a ureter or infundibulum by a calculus.

*Etiology.*—*Age* does not seem to offer much influence in the causation of this disease as it has been found at all ages from intrauterine life to 88 years. Ritchie gives the ages of 75 cases in his table and the average is 45.3 years and the oldest was 88 years, while Jepson operated on a child 4 months and 14 days after birth, which is probably the youngest recorded patient to survive nephrectomy. The number of cases that have been noted at birth is large.

*Sex*, probably has no greater influence. It is unfortunate that the statistics of Ritchie, Lejars and Still are at great variance. Probably neither sex has a predilection for the formation of congeries of renal cysts. Malaria was in a few instances supposed to have an etiological relation. There can be little doubt that a lack of development of the kidney is the principal cause. This takes the form of a failure of coalescences between the branch of the Wolffian duct that changes into the ureter pelvis and calyces of the organ and uriniferous tubules that are formed from the nephrogenic structures in juxtaposition. Obstruction of the ureter or other part of the drainage part of the urinary tract is quite possible, as is either interstitial or parenchymatous nephritis, the one acting by constricting the tubules and the other by blocking them with desquamated epithelium. Nor can the neoplastic origin be entirely ignored.

*Symptomatology.*—Either the onset of the disease is without symptoms other than the presence of a tumor on either side (rarely on only one) increasing in size or they are referable to other organs. In 10 per cent. of the cases no symptoms at any time point to a renal lesion and the diagnosis is made from a

necropsy. Rarely has uremia been the first evidence of renal disease and it has always been promptly followed by coma and death. While dropsical effusions do not occur, the symptoms closely resemble a chronic nephritis. Crises simulating calculous colic occur and not always are such calculi quiescent. There is commonly localized pain and a feeling of fullness in the region of the kidney. The urine behaves much as in chronic nephritis and frequently contains blood as mentioned earlier in this paper; the tumor may become remarkably large, Hare, finding it weighing 16 pounds. Disorders of the nervous system, as well as the gastro-intestinal or the respiratory and circulatory systems are not uncommon.

*Diagnosis.*—The diagnosis is very commonly not made before death. About 10 per cent. of the patients have no symptoms referable to the kidneys and in a larger per cent. of cases uremia was followed rapidly by coma and death. One-fourth of them presents a tumor of the kidney and fully one-half complains of symptoms of chronic nephritis. Lejars found in his series of 62 cases the diagnosis before death was made in but 5. Morris says: "When, with a sallow complexion, hypertrophy of the heart and increased arterial tension, the urinary symptoms mentioned and a tumor in each of the renal regions, or a tumor in one and an increased fullness in the other, are found, the diagnosis of 'large cystic kidney' is pretty clearly indicated." Osler believes hematuria, with characteristics of the urine present, resembling those of chronic interstitial nephritis, together with the presence of bilateral tumors in the flanks and the cardiovascular changes present, should justify the diagnosis of bilateral polycystic kidney. I am prepared to accept this statement, but in the few cases in which the disease is unilateral, or in which, on one side practically no tumor is present the diagnosis is by no means certain. Should developmental abnormalities exist in other portions of the body the presumption

of polycystic kidney is greater and if the patient be an infant the probability is greatly enhanced.

*Prognosis.*—The duration of bilateral polycystic kidney is markedly variable, inasmuch as it causes death in infancy and has been encountered as late in life as 88 years. If these aged subjects have the disease at birth then it is at once understood that the progress is by no means regular. Whether, like adrenal "rests" in the kidney, this degeneration may be dormant for many years and then develop rapidly, is unsettled, but presumably such process does occur. It may lie dormant, apparently during a natural lifetime death occurring from some independent condition. Or, it may rapidly progress, cutting down the patient with but a few days or hours of severe illness, as does chronic interstitial nephritis. In about half the deaths from this disease uremia, coma or convulsions had preceded. Several died from pulmonary or cardiac complications. Cerebral hemorrhage is listed as a forerunner of the fatality and many have died after removal of one kidney.

*Treatment.*—Notwithstanding the deprecating reference made by Osler ("In these operating days, etc.") to modern surgery, neither he nor others have any non-surgical treatment of value to suggest. While a few cases of polycystic kidney apparently have been cured by nephrectomy, Henry Morris, who has written a very fine treatise on "large polycystic kidney," in his excellent "Surgical Diseases of The Kidney and Ureter," says of the five cases he subjected to operation, "Unsatisfactory as these results are, yet two out of the five patients have had their lives prolonged and in complete comfort by nephrectomy, in one case for nearly seven years and in the other for three years. In the third case of unilateral disease the patient might have recovered and survived for years like the other two had he not, so to speak, died an accidental death by suffocation whilst vomiting." About

40 cases of nephrectomy for polycystic kidney with about 20 fatal results are to be found in literature.

It is quite evident that if surgery has naught to offer for the relief of this condition we have but to remain quiet and allow death to claim its victims. It is also perfectly clear to my mind that in the bilateral character of the disease, and nearly always it is bilateral, surgery has little to offer. Beck proposed to incise the cysts, injecting into each small one a drop of saturated solution of iodoform in ether and excision of the large ones. I am not prepared to speak authoritatively, but the difficulty of putting a drop of anything into each of the thousands of cysts in one such kidney or even puncturing each is at once apparent, nor could reliance be placed upon the efficacy of such a measure to prevent refilling of such cysts, as complete obliteration would seem a necessity.

It is quite evident that in those cases successfully subjected to operation and have lived comfortably for some years—perhaps are yet living—the fellow kidney was normal, for in several subjected to nephrectomy, prospects were bright for a few days and then uremia supervened and continued until death shortly ensued. Of this character was Beck's case in which the fellow kidney was small, but rapidly increased in size until death occurred on the eleventh day after operation, Haynes lost his patient two weeks after operation. And here again one is tempted to suggest the probable cause in these successful cases was an obstruction of local character and removable by operation. Certainly no case is recorded of continued improvement in health after any operation on one side when the disease coexisted, to an extent, no matter how slight, on the other side.

Others have operated removing a large polycystic kidney and a rapidly supervening autopsy revealed the opposite kidney in a similar condition. In fact, in one of the ten cases studied by Neate (Kelley's), the right

kidney, weighing 21 1-2 ounces, was removed before death and the left, weighing 23 ounces, by autopsy. The fact that the disease is nearly always bilateral and that it is uncommon to find the disease advanced equally on both sides are very important in considering the advisability of nephrectomy. Another important desideration is that the presence of the tumor or of polycystic kidney is not the fountain of danger necessarily, but, instead, it is the crippling of the excretory work of the two kidneys. Unlike ordinary or malignant renal tumors that are originally unilateral and in which the fellow kidney is usually normal, we here have to deal with a kidney affection practically always double. It seems but logical, then, that our first thought in treatment should be conservation of renal functional structure. In my case Neate estimated that but one-fifteenth of the functioning structure of either kidney remained. It was plain, therefore, as the patient died of deficiency of renal excretion, that it would appear this reduction was too great to be consistent with life. It is then plain that more than two-fifteenths of the functional ability of one kidney must be retained. Just how much more has not been ascertained. But making due allowance for the tendency to rapid progress in the kidney remaining after nephrectomy, it would seem very hazardous to remove a kidney when the other one offers the slightest evidence of involvement.

To sum up then I would say the treatment is non-surgical, except in two conditions. First, when the disease is unilateral or reasonably concluded to be so, and, second, when the cysts are so large as to be burdensome in any way. In the former, incision, or possibly nephrectomy is advisable. If the ureter or other part of the purely waste bearing portion of the corresponding half of the urinary tract be hopelessly obstructed beyond a period of six weeks the function of the corresponding kidney will be permanently suspended and nephrectomy is preferable to incision or multiple